UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/726,193	11/29/2000	Chih-Ming Chen	300.1023	6199

23280 7590 06/29/2006

DAVIDSON, DAVIDSON & KAPPEL, LLC
485 SEVENTH AVENUE, 14TH FLOOR
NEW YORK, NY 10018

EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/726,193	CHEN ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6,8-20,24-33 and 35-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6,8-20,24-33 and 35-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/17/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of IDS filed 4/17/06, request for reconsideration and remarks filed 4/07/06. Claims 1, 4, 6, 8-20, 24-33 and 35-39 are pending. No claim is amended in this submission filed 4/07/06.

Claim Rejections - 35 USC § 103

1. Claims 1, 4, 6, 8-20, 24-33 and 35-39 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Barry et al. (US 5,055,306).

Barry discloses sustained release formulation (abstract; column 3, lines 37-41) and a class of drugs that can be formulated as the sustained release dosage of Barry is the class of drugs used in diabetes and metformin and tolbutamide are the only antidiabetic agents listed (column 7, lines 36).

The instant claims are directed to sustained release formulation comprising metformin as the sole active agent. The claims then describe the function of the formulation. No specific dosage is claimed. No specific polymers are claimed.

Thus the disclosure of a sustained release formulation where the antidiabetic agents metformin and tolbutamide can be active agents meets the limitation of the broad claim to sustained release formulation where the active agent is metformin, therefore, the broad claim to sustained release metformin formulation reads on the disclosure of Barry. With respect to the function or property of the metformin formulation, it is noted as stated in MPEP 2112.02 [R-2] II, "Products of identical chemical composition can not have mutually exclusive properties." A

chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)."

Therefore, administration of product/composition that is essentially the same as the claimed formulation would exhibit the properties/functions recited in the pending claims. Absent a showing of factual evidence, the metformin formulation of Barry would have the properties and functions recited in the instant claims.

Although there is no exemplification of the metformin or tolbutamide formulation, there is a disclosure of a sustained release formulation where metformin and tolbutamide are the suggested antidiabetic agents. The list for antidiabetic agents is not exhaustive.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a sustained release formulation. One having ordinary skill in the art would have been motivated to prepare the sustained release formulation dosage forms that are specifically exemplified and those that may not he exemplified if the goal is to formulate any of those that are not exemplified bearing in mind that the prior art cannot exemplify all the possible drugs that can be formulated as such. One having ordinary skill in the art would have been motivated to use tolbutamide or metformin if the desired active agent is an antidiabetic agent with the expectation that the release of metformin or tolbutamide from the formulation would sustained. The release of metformin or tolbutamide from the formulation of Barry would be sustained absent a factual evidence to the contrary. MPEP 2112.01 [R-2] I states, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either

anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). ***"When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not."*** In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). ***Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433."***

Response to Arguments

Applicants argue:

a) 'Barry fails to teach or suggest a sustained release formulation comprising an active agent consisting of metformin or pharmaceutically acceptable salt thereof which provides "an AUC which is increased by the presence of food as compared with administration in the fasting state" according to claims 1, 6, 8, 9, 12, 15, 18, 24 and 27,' and that Barry does not disclose metformin formulation that does not exhibit a decrease in the bioavailability of metformin if taken with food (claim 31) and Barry further fails to disclose the method of claims 33 and 35.

b) Barry's formulation is not substantially the same dosage form as the instant invention and therefore, "the functional limitations presently claimed would not necessarily be present in the dosage forms of Barry;" that Barry exemplifies making granules of active ingredient and microcrystalline cellulose; the granules are coated with solutions of eudragit and hydroxypropylmethylcellulose; makes granules of effervescent base, and then forming tablets containing mixtures of coated granules and effervescent granules.

Applicants then conclude that the Barry tablets contain coated granules; the tablet disintegrates into sustained release granules upon coming in contact with aqueous liquid.

c) The 50th edition of the Physician Desk Reference, pages 752-757, on GLUCOPHAGE, previously cited by the examiner (and submitted as Exhibit 1, applicants state) discusses that food decreases and slightly delays absorption of metformin and therefore, applicants argue, that the prior art teaches away from the instant invention where the bioavailability (as measured by the AUC) of metformin is increased in the presence of food so that one of ordinary skill in the art would have no expectation that a dosage form provide an increase in AUC and bioavailability as required by the instant claims; that, there is no teaching or suggestion in Barry that would lead one to expect different results than that which is already known in the art.

d) Claims 33 and 35 --- Barry does not disclose the method recited in claims 33 and 35; Barry teaches away from the method of claims 33 and 35 so that the person of ordinary skill in the art would not be motivated to treat a "human patient comprising swallowing an intact controlled release dosage form.

2. Applicants' arguments filed 4/15/06 have been fully considered but they are not persuasive.

In general, claims 1 and 4 are directed composition sustained release comprising metformin or pharmaceutically acceptable salt of metformin as the sole active agent and the claims recite the function/property of the metformin formulation. Claims 6-20, 24-32 are also sustained release formulation comprising sustained release material and metformin as the sole active agent and the claims recite the function/property of the formulation, these claims also

indicate what would happen to the formulation or the property/function of the formulation when it is administered to a patient in the presence of food. It is noted that no specific dosage form (tablet or capsule or suspension of syrup or liquid, for example) is claimed as it regards to the dosage form, amounts of the active agent, specific materials that would provide sustained release. Thus, any sustained release formulation having metformin as the sole active agent would have the property/function of the claimed formulation. In the same manner, a metformin formulation of the prior art having metformin as the sole active agent would undergo the same fate as that of the instant claims formulation upon oral administration in the presence of food.

Regarding a), it is noted that the sustained release formulation of Barry containing metformin as the active agent would have the function/property ascribed and claimed according to the claims. Regarding claims 33 and 35, it is noted that the formulation of Barry is orally administered and the oral administration involves swallowing and because the drugs are the same and the method step is the oral administering, which involves swallowing, the metformin would provide the same effect as that which is claimed. Therefore, Barry discloses the method of claims 33 and 35.

Regarding b), it is noted that the Barry's formulation is substantially the same as that which is claimed and therefore would necessarily have the functions presently claimed. The comprising language of the claims is open and does not exclude coated granules or effervescent tablets as argued by the applicants. Also, it is noted that Barry specifically discloses that metformin is one of the drugs formulated in an easily swallowed sustained release form (column 7, lines 4 and 5 and 36). Barry describes effervescent and water dispersible tablets as conventional non-sustained-release forms (column 8, lines 1 and 2).

Regarding c), it is noted that no exhibit 1 is found with the present response. However, with regards to applicants' citation of the 50th edition of the Physician Desk reference, it is noted that the Glucophage in the 50th edition of the PDR is a specific dosage form and the bioavailability is determined on a 500 mg metformin-HCl tablet. No specific dosage is claimed in the instant claims.

Regarding d), the method of claim 33 orally administers metformin to a patient, and claim 35 to a human, and the formulation is swallowed. The formulation of Barry is also swallowable as discussed above. The formulation is sustained release. No specific dose or dosage is claimed. Barry does not teach away from a swallowable formulation since Barry contemplates the tablet to be swallowed. A tablet that disintegrates orally is also ultimately swallowed. Barry talks about effervescence when the reference talks about conventional non-sustained release forms as described above.

Therefore, the rejection is maintained. No factual evidence was provided to show that the metformin formulation of Barry suffers from all the drawbacks alluded to by applicants in the remarks.

3. The following prior art were made of record in the last office action and although not relied upon, the prior references are considered pertinent to applicants' disclosure.

Pentikainem (in International Journal of Clinical Pharmacology, Therapy and Toxicology, Vol. 24, No. 4, 1986, pp. 213-220) discloses studies comparing sustained release products of metformin (D, C, E0 with rapidly dissolving tablet (B) and aqueous solution (A).

McCarty et al. (US 5,914,326) discloses sustained release metformin formulation (column 4, lines 21, 43 and 44, claims 7, 14 and 16).

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
Tech. Center 1600